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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,651	05/03/2001	Jay M. Short	DIVER1280-12	7330

7590 12/16/2002  
Lisa A. Haile, Ph.D.  
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San Diego, CA 92121-2189

EXAMINER

LOEB, BRONWEN

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 12/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/848,651	<b>Applicant(s)</b> SHORT ET AL.	
	<b>Examiner</b> Bronwen M. Loeb	<b>Art Unit</b> 1636	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 January 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 May 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____          |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                               | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)         |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2&amp;6</u> . | 6) <input checked="" type="checkbox"/> Other: See <i>CONTINUATION</i> on next page. |

### DETAILED ACTION

This action is in response to the communication regarding the sequence dated 18 January 2002.

Claims 1-15 are pending.

### *Sequence Compliance*

1. The specification has been amended to recite SEQ ID Nos. 1 and 2 on p. 66 in accordance with p. 69 in parent application serial number 08/876,276.
2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers, no computer readable format (CRF) was filed, no paper sequence was filed and no attorney statement was filed. These sequences include **the EcoRI linkers on p. 25 [0077]**. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

A reply to a notice to comply with the sequence rules should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office because mail sent to this zip code is destined for irradiation. Computer readable formats, such as disks and CD's, are destroyed as a result of the irradiation process. The following information is also provided on the website.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio  
(<http://www.uspto.gov/ebs/efs/downloads/documents.htm>  
>, EFS Submission User Manual - ePAVE)

2. Mailed to:  
**U.S. Patent and Trademark Office**  
**Box Sequence, P.O. Box 2327**  
**Arlington, VA 22202**

3. Mailed by Federal Express, United Parcel Service or other  
delivery service to:  
**U. S. Patent and Trademark Office**  
**2011 South Clark Place**  
**Customer Window, Box Sequence**  
**Crystal Plaza Two, Lobby, Room 1B03**  
**Arlington, Virginia 22202**

4. Hand Carried directly to the Customer Window at:  
**2011 South Clark Place**  
**Crystal Plaza Two, Lobby, Room 1B03, Box Sequence,**  
**Arlington, Virginia 22202**

***Priority***

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § (120 or 119(e)) as follows:

The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to

comply with the requirements of the first paragraph of 35 U.S.C. §112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

Upon review of the specification of the parent (or provisional) application and comparison with the specification of the present application, it is determined that the specification of parent (or provisional) application 08/876,276 is not enabling for the use and preparation of the instantly claimed invention. The specification of the parent (or provisional) application does not teach or suggest screening for an agent that modulates the interaction of a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety. The specification teaches screening prokaryotes for new bioactive molecules using FACS and co-encapsulation. Since screening for an agent that modulates the interaction of a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety is not disclosed in the parent (or provisional) application and cannot be predicted from the teachings of the parent (or provisional) application, the parent (or provisional) application is not enabling for the instantly claimed invention. Thus, the requirements of the first paragraph of 35 U.S.C. §112 have not been met. Accordingly, claims 1-15 are assigned an effective filing date of 16 June 1998.

#### ***Specification***

4. The disclosure is objected to because of the following informalities: In the Abstract, the word "nucleic" is misspelled on line 3.

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On pp. 10-11, [0026-0027], a “ $\beta$ ” was amended in three instances by informal Examiner’s amendment in place of the “b” in the term “b-galactosidase” or in place of a blank in the term “–galactosidase”.

On p. 16 [0045] the unknown term “(library” is used. Is this a typographical error?

On p. 27 [0082] the unknown term “(-factor” is used. Is this a typographical error?

On p. 38 [0136] the unknown term “(-ZAP vectors” is used. Is this a typographical error?

On p. 41 [0147] and p. 43 [0149], the unknown term “fluorescein-di-(-D-galactopyranoside” is used. Is this a typographical error?

On pp. 41-42, [0147-0148], a “ $\beta$ ” was amended in seven instances by informal Examiner’s amendment in place of the “(“ in the term “(-galactosidase”.

On p. 54 [0185] there is a reference to “Figure X” however there is no such figure provide. Also, there appears to be a typographical error in the phrase “which can the be decorated”; should it be “then”?

On p. 56 [0189] in the phrase “liquid grown culture”, should it actually be “growth”?

On p. 57 [0197] line 2 the phrase “compounds can are utilized” is grammatically incorrect.

On p. 64, the table in [0214] is cut off on the far right side.

On pp. 69-70 [0238] the recited references would be better listed with each reference starting a new paragraph as was done in [0234]-[0237].

Appropriate correction is required.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

### ***Drawings***

5. The drawings are objected to because in Figure 7, "fluor" is misspelled; Figure 14 states "from host" whereas in the Brief Description of the Drawings, it appears that the correct phrase should be "the library"; and in Figure 15 "growth" is misspelled. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

### ***Claim Objections***

6. Claim 1 is objected to because of the following informalities: Claim 1 recites the abbreviation "FACS" without providing a definition; an abbreviation should be defined at its first recitation in the claim set. Appropriate correction is required.

7. Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

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required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 15, ultimately dependent on claim 1, recites "wherein detection of the fluorescent dye or a visible dye is carried out by fluoremetric or spectrophotometric measurement" however claim 1 already recites the use of FACS analysis for detection. Thus the recitation in claim 15 actually broadens the scope of the parent claim.

### ***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 10 rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 1 is drawn to a method for screening an agent that modulates (either enhancing or inhibiting) the interaction of a first test protein and a second test protein. This is a genus claim in terms of any first and second test proteins. The specification mentions screening for agents that enhance or inhibit ligand and receptor interactions



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(p. 50 [0179]). This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all first and second test proteins based on the teachings in the specification. The specification discloses using receptors and their ligands including membrane bound G-protein receptors and ligands (pp. 50-51 [0179]). While there are numerous protein ligands and receptors known (for instance insulin and its receptor and luteinizing hormone and its receptor), the claimed genus is not restricted to membrane bound G-protein receptors and ligands and therefore encompasses any combination of a first and second test protein. This genus therefore encompasses a vast number of species. Therefore, the specification does not describe the claimed first and second test proteins in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these proteins at the time of filing the present application. Thus, the written description requirement has not been satisfied.

10. The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-15 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite as there is no clear nexus between “determining the ability of the agent to modulate the interaction of the first test protein linked to a DNA binding moiety with the second test protein covalently linked to a transcriptional

activation moiety” and “the agent enhances or inhibits the expression of a detectable protein”.

Claim 1 is vague and indefinite because the preamble recites “screening for an agent that modulates the interaction of a first test protein linked to a DNA binding moiety and a second test protein linked to a transcription activation moiety” and the concluding wherein phrase “wherein the agent enhances or inhibits the expression of a detectable protein”. It would appear the method steps do not achieve the intended goal of the method.

Claim 4 is vague and indefinite in reciting “the agent inhibits the activity of the first protein or the second protein”. The parent claim is directed to screening for an agent that modulates the interaction between a first and second protein, not for an agent that inhibits activity.

Claim 5 is vague and indefinite in reciting “the agent enhances the activity of the first protein or the second protein”. The parent claim is directed to screening for an agent that modulates the interaction between a first and second protein, not for an agent that enhances activity.

Claim 6 recites the limitations “the recombinant cell” and “the target protein and detectable marker” in lines 1-2. There is insufficient antecedent basis for these limitations in the claim.

Claim 6 is vague and indefinite in reciting “a recombinant cell co-encapsulated with **the** recombinant cell (emphasis added)”. Antecedent basis would indicate that the second cell is the same as the first cell, however, it appears that Applicant is actually

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referring to two different recombinant cells. This rejection would be overcome by amending claim 6 to recite "wherein the agent is expressed from a second recombinant cell" and also by amending claim 1 to provide antecedent basis for the phrase "the recombinant cell expressing the target protein and detectable marker".

Claim 7 is vague and indefinite as it is unclear to which of the two recombinant cells the phrase "the recombinant cell" refers.

Claim 8 is vague and indefinite as it is unclear to which of the two recombinant cells the phrase "the recombinant cell" refers.

Claim 13 recites the limitation "the detectable marker" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 13 is vague and indefinite as it is unclear how FACS, as recited in independent claim 1, can be used with non-fluorescent materials, such as a visible dye, a chemiluminescent material, a radioactive material or any enzymatic substrate which does not fluoresce.

***Claim Rejections - 35 USC § 102***

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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13. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

15. Claims 7 and 8 are examined assuming that "the recombinant cell" is the cells expressing the two hybrid proteins and the detectable protein.

16. Claims 1, 7, 9, 13 and 15 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Mendelsohn et al (Current Opinion in Biotechnology (1994) 5:482-486).

Mendelsohn et al teach using two-hybrid systems to identify compounds that modulate protein interactions. In a typical two-hybrid system, a first protein is linked to a DNA-binding domain and a second protein is linked to transcriptional activation domain wherein when the first and second proteins interact, transcriptional activation occurs of a reporter gene. Modulation of the protein interaction results in changes in

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transcriptional activation. Both fusions are encoded by expression constructs which are co-encapsulated in a cell. Use of a fluorescent reporter system, such as green fluorescent protein or lacZ in combination with a fluorescent substrate is taught.

Quantitating the expression of the fluorescent reporter using automated equipment is taught. Use of two-hybrids in either yeast or mammalian cells is disclosed. See entire document, especially pp. 482-484 "Two-hybrid Systems" and p. 485, first column, 2<sup>nd</sup> paragraph). If the use of FACS in the two-hybrid screening taught by Mendelsohn et al is not inherent in the teaching of using automated equipment, it would have been obvious to one of ordinary skill in the art at the time of filing. One of ordinary skill in the art would have motivated to used FACS in the method taught by Mendelsohn et al because Mendelsohn et al teach using fluorescent molecules as the reporter system, teach the used of automated equipment in quantitating the fluorescent reporter molecules (with the advantage of the ease of using automated equipment) and FACS is an extremely well-known automated means of detecting a fluorescent reporter system.

17. Claims 1-3, 5, 7, 9 and 13-15 are rejected under 35 U.S.C. §103(a) as being unpatentable over Anderson et al (USP 5,968,738) in view of Young et al (Biology of Reproduction (1998) 58:302-311).

Anderson et al teaches two-hybrid assays in mammalian cells using FACS-analyzable reporter molecules. The reporter molecules are green fluorescent proteins modified so that they can be used in mammalian cells. See entire document, especially col. 7, lines 3-17m col. 8, lines 15-25 and claim 11.

Young et al is a review article about two-hybrid assays and their wide applicability. Young et al teaches that among the many uses for two-hybrid assays there is drug discovery, specifically identifying agents that affect protein-protein interactions. Such agents may be obtained for instance from compound banks or may be a third protein co-expressed with the two-hybrid fusion proteins. See entire document, p. 304, first column, third full paragraph, and p. 308-309 under "Drug Discovery" and "High-Throughput Screening".

At the time the invention was filed, it would have been obvious to one of ordinary skill in the art to use the two-hybrid assay taught by Anderson et al to screen for agents that modulate protein-protein interactions as taught by Young et al. One of ordinary skill in the art would have been motivated to do so in order to screen for potential therapeutics (which advantageously would target specific molecular interactions) from large compound banks in the rapid, automated way FACS analysis permits. One of ordinary skill in the art would have reasonably expected success in practicing such a combination.

### ***Conclusion***

Claims 1-15 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's

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representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 11:00 AM to 7:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bronwen M. Loeb, Ph.D.  
Patent Examiner  
Art Unit 1636

December 9, 2002



JAMES KETTER  
PRIMARY EXAMINER

Application serial no. 09/848,651

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date

Certificate of Mailing Date

5 March 2002

20 February 2002 Paper #5

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

**COPY OF PAPERS  
ORIGINALLY FILED**

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 7



## Notice to Comply

**Application No.**

09/848,651

**Examiner**

Bronwen M. Loeb

**Applicant(s)**

SHORT ET AL.

**Art Unit**

1636

### NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: See CONTINUATION on next page

#### Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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**PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY**

Box 6 CONTINUATION: Copy of Papers Originally Filed information and Revised Notice to Comply

Box 7 CONTINUATION:

On p. 25 [0077] there is a sequence that lacks a sequence identifier. If this sequence is already in the paper listing and computer readable form (CRF) of the sequence listing, Applicant only needs to amend the specification to disclose the SEQ ID No. If however this sequence is not in both the paper listing and the CRF, the following items need to be provided.